SETBP1 disorder

SETBP1 disorder is a condition that involves speech and language problems, intellectual disability, and distinctive facial features.

In people with SETBP1 disorder, problems with expressive language skills (vocabulary and the production of speech) are generally more severely affected than receptive language skills (the ability to understand speech). Speech development may be limited to a few words or no speech. Affected individuals often communicate using gestures or by mimicking the expressions of others.

Individuals with SETBP1 disorder have intellectual disability that can range from mild to moderate. They may also have behavioral problems, such as attention-deficit/hyperactivity disorder (ADHD) or autistic behaviors that affect communication and social interaction. Affected individuals may have weak muscle tone (hypotonia); delayed development of motor skills, such as sitting, standing, and walking; or recurrent seizures (epilepsy).

Distinctive facial features in people with SETBP1 disorder can include a long face, a high forehead, eyebrows that grow together in the middle (synophrys), short eye openings (short palpebral fissures), skin folds covering the inner corner of the eyes (epicanthal folds), droopy eyelids (ptosis), puffiness of the skin around the eyes (periorbital fullness), small nostrils, a high nasal bridge, a broad tip of the nose, a thin upper lip, a high arch in the roof of the mouth (high-arched palate), and a small chin.

Frequency

The exact prevalence of SETBP1 disorder is unknown, although it is thought to be a rare disorder. At least 45 affected individuals have been described in the scientific literature.

Causes

SETBP1 disorder is caused by mutations in the *SETBP1* gene. This gene provides instructions for making a protein that attaches (binds) to certain regions of DNA to increase gene activity (expression). The SETBP1 protein is found throughout the body, but protein levels are highest during brain development before birth. During this time, nerve cells grow and divide (proliferate) and move (migrate) to their proper location in the brain. The SETBP1 protein is thought to control the activity of genes involved in these developmental processes.

SETBP1 gene mutations that cause SETBP1 disorder prevent the production of any functional SETBP1 protein. It is unclear how the loss of SETBP1 protein leads to the specific features of SETBP1 disorder. A shortage of this protein probably impairs the

expression of certain genes in the brain, disrupting development. Abnormalities in certain brain regions likely underlie the speech, intellectual, and behavioral problems that can occur in SETBP1 disorder.

Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Most cases of this condition result from new (de novo) mutations in the gene that occur during the formation of reproductive cells (eggs or sperm) in an affected individual's parent or in early embryonic development. These cases occur in people with no history of the disorder in their family.

Other Names for This Condition

- mental retardation, autosomal dominant 29
- MRD29
- SETBP1 related developmental delay
- SETBP1-related disorder
- SETBP1-related intellectual disability

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Mental retardation, autosomal dominant 29
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C4015141/

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Intellectual Disability
  https://medlineplus.gov/ency/article/001523.htm
- Encyclopedia: Speech Disorders--Children
  https://medlineplus.gov/ency/article/001430.htm
- Health Topic: Developmental Disabilities
  https://medlineplus.gov/developmentaldisabilities.html
- Health Topic: Speech and Language Problems in Children
  https://medlineplus.gov/speechandlanguageproblemsinchildren.html

Genetic and Rare Diseases Information Center

- SETBP1 disorder
  https://rarediseases.info.nih.gov/diseases/13379/setbp1-disorder

Additional NIH Resources

- National Institute on Deafness and Other Communication Disorders: Speech and Language Developmental Milestones
  https://www.nidcd.nih.gov/health/speech-and-language

Educational Resources

- Centers for Disease Control and Prevention: Language and Speech Disorders in Children
  https://www.cdc.gov/ncbddd/childdevelopment/language-disorders.html
- Kennedy Krieger Institute: Developmental Disorders
  https://www.kennedykrieger.org/patient-care/conditions/developmental-disorders
- MalaCards: setbp1 disorder
  https://www.malacards.org/card/setbp1_disorder
- Merck Manual Consumer Version: Communication Disorders in Children
  https://www.merckmanuals.com/home/children-s-health-issues/ear,-nose,-and-throat-disorders-in-children/communication-disorders-in-children
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/setbp1-disorder/

Patient Support and Advocacy Resources

- Child Neurology Foundation
  https://www.childneurologyfoundation.org/
- SETBP1 Society
  http://www.setbp1.org/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28SETBP1+disorder%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- MENTAL RETARDATION, AUTOSOMAL DOMINANT 29
  http://omim.org/entry/616078

Medical Genetics Database from MedGen

- Mental retardation, autosomal dominant 29
  https://www.ncbi.nlm.nih.gov/medgen/863578

Sources for This Summary

- Coe BP, Witherspoon K, Rosenfeld JA, van Bon BW, Vulto-van Silfhout AT, Bosco P, Friend KL, Baker C, Buono S, Vissers LE, Schuurs-Hoeijmakers JH, Hoischen A, Pfundt R, Krumm N, Carvill GL, Li D, Amaral D, Brown N, Lockhart PJ, Scheffer IE, Alberti A, Shaw M, Pettinato R, Tervo R, de Leeuw N, Reijnders MR, Torchia BS, Peeters H, O'Roak BJ, Fichera M, Hehir-Kwa JY, Shendure J, Mefford HC, Haan E, Gécz J, de Vries BB, Romano C, Eichler EE. Refining analyses of copy number variation identifies specific genes associated with developmental delay. Nat Genet. 2014 Oct;46(10):1063-71. doi: 10.1038/ng.3092. Epub 2014 Sep 14.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/25217958
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4177294/
- Filges I, Shimojima K, Okamoto N, Röthlisberger B, Weber P, Huber AR, Nishizawa T, Datta AN, Miny P, Yamamoto T. Reduced expression by SETBP1 haploinsufficiency causes developmental and expressive language delay indicating a phenotype distinct from Schinzel-Giedion syndrome. J Med Genet. 2011 Feb;48(2):117-22. doi: 10.1136/jmg.2010.084582. Epub 2010 Oct 30.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21037274
- Marseglia G, Scordo MR, Pescucci C, Nannetti G, Biagini E, Scandurra V, Gerundino F, Magi A, Benelli M, Torricelli F. 372 kb microdeletion in 18q12.3 causing SETBP1 haploinsufficiency associated with mild mental retardation and expressive speech impairment. Eur J Med Genet. 2012 Mar;55(3):216-21. doi: 10.1016/j.ejmg.2012.01.005. Epub 2012 Jan 25.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22333924
- Perdue MV, Mascheretti S, Kornilov SA, Jasinska KK, Ryherd K, Einar Mencl W, Frost SJ, Grigorenko EL, Pugh KR, Landi N. Common variation within the SETBP1 gene is associated with reading-related skills and patterns of functional neural activation. Neuropsychologia. 2019 Jul;130: 44-51. doi: 10.1016/j.neuropsychologia.2018.07.015. Epub 2018 Aug 23.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/30009840
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6542718/

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/condition/setbp1-disorder

Reviewed: August 2019
Published: June 23, 2020

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services